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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,417	03/04/2002	Bernd Riedl	BAYER 16 P4	3172

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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	9

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,417	RIEDL ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2002 and 08 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 39-53* is/are pending in the application.

4a) Of the above claim(s) *2,5,6,12 and 39-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 7-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The following is responsive to the preliminary amendment received March 4, 2002 and Applicant's election received Aug. 8, 2003.

Claims 13-38 are cancelled. New claims 39-53 are added. Claims 1-12 and 39-53 are currently pending.

Applicant's election, with traverse, of compound C1a (page 50 of the specification) with a further election of arthritis is acknowledged. The traversal is on the ground(s) that the Examiner has not shown undue burden to examine the use of diaryl ureas as a class, in treating p38-mediated diseases.

Said argument has been considered but is not found to be persuasive. The claims require the treatment of numerous diseases by the administration of a compound represented by formula (I), wherein the compound of formula (I) encompasses numerous compounds containing cyclic, aryl and heteroaryl moieties. The compounds encompassed by formula (I) are each chemically and structurally distinct and the search for one would not be required for the other. Concerning the election of a specific disease, the Examiner respectfully submits that each disease disclosed and claimed by Applicant is distinct and the search for one would not be required for the other.

The election is therefore maintained.

No prior art was found for the elected compound in a method of treating arthritis. Therefore, the search was expanded to another species within formula (I) for use in a method for treating arthritis.

Claims 2, 5, 6, 12, 39-53 are withdrawn from consideration.

Information Disclosure Statement

Applicant's Information Disclosure Statement received April 2, 2002 has not been considered. It appears that no copies of the listed references have been submitted. Pursuant to 37 CFR 1.98, Applicant is respectfully requested to submit copies of the US patent documents and the foreign patent documents.

Claim Objections

1. Claim 4 is objected to because of the following informalities: in claim 4, "birth control" should be deleted because it is not a disease. Appropriate correction is required.

Claim Rejections—35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 3, 4, 7-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the

predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The claims are drawn to methods of treating a disease mediated by p38 within a host by administering to the host a compound represented by formula (I).

(2) **The state of the prior art**

The art recognizes the usefulness in developing inhibitors of p38 in order to treat diseases associated with p38 such as allergies, cancer, etc. Please see Salituro et al., col. 1, lines 34-58. Salituro et al. disclose that although compounds that specifically inhibit p38 have been developed, the efficacy of these inhibitors *in vivo* is still be investigated. Please see col. 1, lines 54-58.

(3) The relative skill of those in the art

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical and chemical art is high.

(5) The breadth of the claims

The claims are broad and encompass treatment of numerous diseases associated with p38 by administering a vast number of compounds, which differ chemically and structurally.

(6) The amount of direction or guidance presented

Applicant's specification does not provide guidance for the treatment of diseases mediated by p38 using the compounds encompassed by formula (I). The specification provides no guidance to enable one of ordinary skill in the art to use the invention commensurate in scope with the claims, which, as stated above, are broad and encompass numerous diseases and compounds, which differ chemically and structurally. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." Applicant's specification does not set forth a representative number of examples of compounds capable of carrying out the claimed methods. While the specification provides a number of specific compounds preferred by Applicant for use in the claimed methods, these compounds are not representative of the huge scope of compounds encompassed by formula (I).

(7) The presence or absence of working examples

There are no working examples in the specification relating to the treatment of the claimed diseases. The only working examples described are a p38 kinase assay and a murine LPS induced TNF-alpha production *in vivo* model. The specification lacks a representative number of working examples, which would guide and thus enable one of ordinary skill in the practice the invention commensurate in scope with the claims.

(8) The quantity of experimentation necessary

Therefore, since (1) Salituro et al. suggest that p38 inhibitory activity of a compound does not necessarily translate into in vivo efficacy, (2) since the claims encompass treatment of numerous diseases by the administration of numerous compounds which differ structurally and chemically, (3) since the specification lacks guidance and/or working examples which would enable one of ordinary skill in the art to practice the invention commensurate in scope with the claims, and (4) since compound structure and activity for pharmaceutical use must be determined from case to case by painstaking experimental study, one of ordinary skill in the art would be burdened with undue experimentation to determine which compounds encompassed by formula (I) would be capable of treating the large number of disorders mediated by p38.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 4, 7, 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 4 recites the limitation "the condition" in line 1. There is insufficient antecedent basis for this limitation in the claim.

5. Claim 7 recites the limitation "wherein M is one or more bridging groups" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections—35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 3, 4, 7-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salituro et al., 6,093,742. (cited in IDS received April 2, 2002).

Salituro et al. disclose p38 inhibitors useful in methods for treating disorders such as inflammation or autoimmune diseases, such as rheumatoid arthritis. Specifically, the method comprises treating rheumatoid arthritis by administering a compound represented by formula (I), with a preferred compound being compound 20 disclosed at col. 8. Please see the abstract; col. 2, lines 1-45; col. 8, compound 20; col. 40, lines 36-38.

Salituro et al. do not specifically disclose that the phenyl groups of compound 20 are substituted as required by the claims; however, the Examiner refers to col. 2, lines 1-40, where Salituro et al. teach that the aromatic rings may be optionally substituted with substituents such as $CON(R^3)_2$; COR^3 or SO_2NR^3 .

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the phenyl groups of compound 20 not only because Salituro et al. suggest such a substitution but also because one of ordinary skill in the art would reasonably expect the resulting modified compound to maintain its p38 inhibitory activity, thereby treating patients suffering from rheumatoid arthritis.

Conclusion

Claims 1, 3, 4, 7-11 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is 571-272-0572. The examiner can normally be reached on Mon-Fri from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (571) 272-0584. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

CDM

Feb. 8, 2004

Cybille Delacroix-Muirheid
Patent Examiner Group 1600